

REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicants appreciate the Examiner's allowance of claims 28 through 35, 38, 40, 41, 49 and 50.

Applicants note that the Examiner has allowed claims 28 through 35 which include all of the generic compound claims, covering the compounds of the Formula (I) as well as the subgeneric compounds of the Formulae (IA), (IB) and (IC). Claims 38, 40 and 41 directed to ultimate species within the scope of the Formula (I) have also been allowed. The remaining compound claims 36, 37, and 39 directed to species have been rejected only because of some informalities. Applicants have canceled claims 36, 37 and 39 and replaced those claims respectively with claims 55, 56 and 57 so that all of the compound claims should be in condition for allowance.

The Examiner has not as yet allowed a broad claim directed to a process for preparing the new compounds of the Formula (I). Independent process claim 42 has been rejected, but has been rejected only on the grounds that the claim is indefinite. Applicants have canceled process claim 42 and dependent process claims 43 through 46 and replaced those claims with new claims 58 through 62, so that all of the process claims should be in condition for allowance as well.

The Examiner has also allowed pharmaceutical composition claim 49 and method of treatment claim 50 which are both directed to Formula (I) compounds for the treatment of epilepsy. The Examiner is satisfied that the specification supports that the new compounds of the Formula (I) have this utility. However, the Examiner will not agree that pharmaceutical composition claims 47, 51 and 53 and method of treatment claims 48, 52 and 54 are adequately supported by the disclosure. Claims 51 and 52 relate to the new Formula (I) compounds and their use in the treatment or prevention of stroke, Parkinson's disease, multiple sclerosis, or amyotrophic lateral sclerosis. The Examiner has accepted that the new Formula (I) compounds are useful in treating stroke and amyotrophic lateral sclerosis, but has not accepted that the compounds are useful to treat Parkinson's disease or multiple sclerosis without further proof that the specific presently claimed compounds are effective to treat these diseases.

Applicants are submitting a second Declaration under 37 CFR 1.132 of Dr. Laszlo G. Harsing, who has either personally conducted or supervised the carrying out of additional tests to establish that the new compounds of the Formula (I) are effective in the treatment of Parkinson's disease and in the treatment of multiple sclerosis. To establish that the new compounds of the Formula (I) are effective in the treatment of Parkinson's Disease, Applicants have obtained test data in rats using the compound of Example 27, namely, (+)-7-acetyl-5-(4-amino-3-methyl-phenyl)-7,8-dihydro-8-methyl-9H-1,3-dioxolo[4,5-h][2,3]benzodiazepin. See Test

1 in the declaration. Applicants have found that administration of the compound of Example 27 to rats successfully reduced catalepsy to about the same extent as where bromocriptine was administered. See the data in Table 1 of the declaration which indicates that the species of Example 27 has an LD50 value almost as low as that of bromocriptine, a known substance for this particular purpose. In view of the data in Test 1 of the new Declaration under 37 CFR 1.132, Applicants have established that their Formula (I) compounds are effective in the treatment of Parkinson's disease and that the pharmaceutical composition claim 51 and the method of treatment claim 52 reciting this utility are supported.

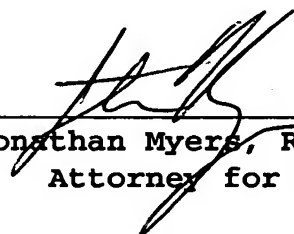
Claims 51 and 52 also recite the treatment of multiple sclerosis. In Test 2 in the declaration Applicants have employed the compound of the Formula (I) in Example 28, namely, (+)-5-(3-methyl-4-amino-phenyl)-7,8-dihydro-8-methyl-7-propionyl-9H-1,3-dioxolo-[4,5-h]-[2,3]benzodiazepine in an experiment in rats to establish the efficacy of the Formula (I) compounds in the treatment of multiple sclerosis. The rats were first immunized subcutaneously with an inoculum containing Mycobacterium tuberculosis which is known to induce autoimmune encephalomyelitis, a manifestation of multiple sclerosis. The compound of the Formula (I) in Example 28 performed well against a reference compound known for this purpose in controlling the inflammation caused by autoimmune encephalomyelitis. Both the compound of Example 28 and the reference compounds were administered to rats i.p. following the immunization with the inoculum. Accordingly Applicants have

established that the present compounds of the Formula (I) are effective both in treating Parkinson's disease and in treating multiple sclerosis and therefore no rejection of claims 51 and 52 should be maintained under 35 USC 112, first paragraph, as based upon a non-enabling disclosure.

The Examiner also maintains that claims 53 and 54 directed to the treatment of any neurodegenerative disease using the new Formula (I) compounds is too broad and beyond the scope of the enabling disclosure provided by the specification. Specifically the Examiner believes that only a limited number of neurodegenerative disorders would be expected to be treated by the new compounds of the Formula (I). Applicants have amended claims 53 and 54 to provide a more limited definition of the diseases to be treated stating that the neurodegenerative disease is one which responds to non-competitive antagonism of an AMPA/cainate receptor. The Examiner indicates that she does not agree that "antagonizing an AMPA/cainate receptor is a per se utility without correlating this activity to the treatment of a particular disease or group of diseases. Applicants' amendments to claims 53 and 54, however, do correlate antagonizing the AMPA/cainate receptor with treating a particular disease or group of diseases, namely, neurodegenerative diseases. Furthermore this correlation is supported by the data in the first and second declarations under 37 CFR 1.132 of Dr. Harsing. Thus no rejection of claims 53 and 54 as now presented should be maintained under 35 USC 112, first paragraph, as based upon a non-enabling disclosure.

Applicants believe that all claims now presented are allowable and a response to that effect is earnestly solicited.

Respectfully submitted,
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Enclosure: Declaration under 37 CFR 1.132